UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/529,342	07/27/2000	DAVID J. CLARKE	39-206	8022

23117 7590 06/23/2008

NIXON & VANDERHYE, PC
901 NORTH GLEBE ROAD, 11TH FLOOR
ARLINGTON, VA 22203

EXAMINER	
YANG, NELSON C	

ART UNIT	PAPER NUMBER
1641	

MAIL DATE	DELIVERY MODE
06/23/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/529,342	CLARKE ET AL.	
	Examiner	Art Unit	
	Nelson Yang	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42-68* is/are pending in the application.

4a) Of the above claim(s) *43,44,53,62,63,67 and 68* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42,45-52,54-61 and 64-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 April 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 3, 2007 has been entered.

Response to Amendment

2. Claims 42-68 are pending.

3. Claims 43, 44, 53, 62, 63, 67, 68 are withdrawn.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 42, 45-49, 51, 64 are rejected under 35 U.S.C. 102(e) as being anticipated by Smith et al. [US 6,344,436] in light of Subbarao et al. [Subbarao et al., pH dependent bilayer destabilization by an amphiphathic peptide, 1987, 26, 2964-2972].

With respect to claim 42, 64, Smith et al. teach peptide-macromolecule complexes for delivering a macromolecule into a cell (see entire document, in particular column 2, lines 62-67), comprising a phospholipid bilayer, receptor ligand for targeting specific cells, and lytic peptides (fig. 1), wherein the lytic peptides disrupts the structural organization of the cell membrane to thereby cause leakage through the endosome into the cytoplasm (column 6, lines 53-65) and which may comprise amphipathic peptides such as GALA (column 7, lines 55-61), wherein the lytic peptides may be associated in a covalent or non-covalent means (column 6, lines 45-52). Although Smith et al. do not explicitly disclose that GALA interacts with the layer to act as or mediate the opening of pores or channels, one of ordinary skill in the art would have known, as evidenced by Subbarao et al. that GALA are peptides attached to the surface of liposomes and interact with bilayers in a pH-dependent fashion (p.2965, col.1, para.2), wherein when the pH is decreased to pH 5, it would promote helix formation within the bilayer (p. 2970, col.1, para. 2), resulting in pores.

6. With respect to claim 45, Smith et al. disclose that the lytic peptides may be associated in a covalent or non-covalent means to the endosome (column 6, lines 45-52).

7. With respect to claim 46, Smith et al. teach a receptor ligand for targeting specific cells (fig. 1).

8. With respect to claim 47, Smith et al. teach that the receptor may be antibodies for binding to antigens (column 10, lines 10-20).

9. With respect to claims 48, 49, Smith et al. teach binding peptides for aggregation (column 8, lines 5-13).

10. With respect to claim 51, Smith et al., teach amphipathic peptides such as GALA (column 7, lines 55-61)

11. Claim 50 is rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al. [US 6,344,436] in light of Li et al [US 5,512,294].

With respect to claim 50, Smith et al. teach peptide-macromolecule complexes for delivering a macromolecule into a cell (column 2, lines 62-67), comprising a phospholipid bilayer, receptor ligand for targeting specific cells, and lytic peptides (fig. 1), wherein the lytic peptides disrupts the structural organization of the cell membrane to thereby cause leakage through the endosome into the cytoplasm of the cell (column 6, lines 53-65) and which may comprise amphipathic peptides such as GALA (column 7, lines 55-61), wherein the lytic peptides may be associated in a covalent or non-covalent means (column 6, lines 45-52). Smith et al. further teach ligands such as biotin (column 10, lines 21-28), which would bind to avidin or streptavidin, as shown by Li et al. In particular, Li et al. demonstrate that teach liposomes where avidin is used to bind proteins such as antibodies, the antibodies are attached by the biotin-avidin biotinylated antibody sandwich (fig.16, column 9, lines 65-67). One of ordinary skill in the art would therefore realize that the biotin ligands of Smith et al. would have to bind to avidin receptors.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claim 52 is rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al. [US 6,344,436].

With respect to claim 52, Smith et al., teach amphipathic peptides such as GALA (column 7, lines 55-61). Since the amino acid sequence of GALA and N, Myristic GALA is essentially the same, with similar functions and pH sensitivities, GALA would be functionally equivalent to N, Myristic GALA and therefore it would be obvious to one of ordinary skill in the art to utilize GALA or N, Myristic GALA, in order permit rapid and complete leakage when GALA lyses the lipid vesicles.

14. Claims 54-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al. [US 6,344,436] in view of Levinson et al [US 6,020,142].

With respect to claims 54-57, Smith et al. teach peptide-macromolecule complexes for delivering a macromolecule into a cell (see entire document, in particular column 2, lines 62-67), comprising a phospholipid bilayer, receptor ligand for targeting specific cells, and lytic peptides (fig. 1), wherein the lytic peptides disrupts the structural organization of the cell membrane to thereby cause leakage through the endosome into the cytoplasm (column 6, lines 53-65) and which may comprise amphipathic peptides such as GALA (column 7, lines 55-61), wherein the lytic peptides may be associated in a covalent or non-covalent means (column 6, lines 45-52).

Smith et al. do not teach that the species is a dye, a substrate for an enzyme, or an enzyme such as glucose oxidase.

Levinson et al, however, teach the use of a delivery complex such as liposomes (column 3, lines 5-12) for delivering enzymes such as glucose oxidase and chromogenic substrates, which are dyes (column 25, lines 40-46), in order to label RATH gene peptide-specific antibodies. This is important as the RATH1.1 gene product has been demonstrated to act as a mediator of signal transduction events, and and the detection of compounds which modulate the RATH gene product would allow for the diagnostic evaluation, prognosis, and treatment of immune disorders involving T cell activation (column 1, lines 29-62).

Therefore one of ordinary skill in the art would have been motivated to have the liposomes deliver enzymes such as glucose oxidase and chromogenic substrates, as suggested by Levinson et al, in the method of Smith et al., to in order to study specific cells such as T cells, such that the diagnostic evaluation, prognosis, and treatment of immune disorders involving T cell activation is possible.

15. Claims 58-59, 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al. [US 6,344,436] in view of Robinson et al [US 5,994,149].

With respect to claims 58, 59, 61, Smith et al. teach peptide-macromolecule complexes for delivering a macromolecule into a cell (see entire document, in particular column 2, lines 62-67), comprising a phospholipid bilayer, receptor ligand for targeting specific cells, and lytic peptides (fig. 1), wherein the lytic peptides disrupts the structural organization of the cell membrane to thereby cause leakage through the endosome into the cytoplasm (column 6, lines

53-65) and which may comprise amphipathic peptides such as GALA (column 7, lines 55-61), wherein the lytic peptides may be associated in a covalent or non-covalent means (column 6, lines 45-52). Smith et al. do not teach the detection of pathogenic cells in foodstuffs.

Robinson et al, however, do teach the analysis of foodstuffs (column 7, lines 39-55) and animals or humans (column 7, lines 29-39) for pathogenic cells using liposomes. Robinson et al further teach that it would be desirable to have a test kit that would eliminate operator error, and have a predictably accurate and reproducible rate of identification of pathogenic fungi, yeasts and molds (column 1, lines 16-45).

Therefore it would be obvious to teach the detection of pathogenic cells in foodstuffs or in animals, as taught by Robinson et al, in the method of Smith et al., in order to have a test kit that would eliminate operator error, and have a predictably accurate and reproducible rate of identification of pathogenic fungi, yeasts and molds.

16. Claims 58, 60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al. [US 6,344,436] in view of Blondin et al [US 4,808,517].

With respect to claims 58, 60, Smith et al. teach peptide-macromolecule complexes for delivering a macromolecule into a cell (see entire document, in particular column 2, lines 62-67), comprising a phospholipid bilayer, receptor ligand for targeting specific cells, and lytic peptides (fig. 1), wherein the lytic peptides disrupts the structural organization of the cell membrane to thereby cause leakage through the endosome into the cytoplasm (column 6, lines 53-65) and which may comprise amphipathic peptides such as GALA (column 7, lines 55-61), wherein the

lytic peptides may be associated in a covalent or non-covalent means (column 6, lines 45-52). Smith et al. do not teach the detection of pathogenic cells in water samples.

Blondin et al, however, do teach a method of using of lipid vesicles (column 4, lines 9-24) for the detection of toxins in water samples (column 8, lines 20-32) that is economical and efficient and can be quickly and easily performed (column 2, lines 64-68).

Therefore it would be obvious to use the method of Smith et al. to analyze water samples for pathogens as taught by Blondin et al, in order to detect toxins economically, efficiently, quickly and easily.

17. Claims 65-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al. [US 6,344,436] in view of Subbarao et al. [Subbarao et al., pH dependent bilayer destabilization by an amphiphathic peptide, 1987, 26, 2964-2972].

With respect to claims 65-66, Smith et al. teach teach peptide-macromolecule complexes for delivering a macromolecule into a cell (see entire document, in particular column 2, lines 62-67), comprising a phospholipid bilayer, receptor ligand for targeting specific cells, and lytic peptides (fig. 1), wherein the lytic peptides disrupts the structural organization of the cell membrane to thereby cause leakage through the endosome into the cytoplasm (column 6, lines 53-65) due to a change in pH (column 7, lines 45-50). Smith et al., however, fail to teach a change from a pH of above 6.0 or 7.0.

Subbarao et al., however, teach that a change in pH from 7.5 to 5.0 results in an increase in the helical content of GALA, thus increasing its ability to bring about leakage in vesicles (p.2965, col.1, para. 3).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to have changed the pH from 7.5 to 5.0 in the method of Smith et al., in order to induce leakage of endosomal contents

Response to Arguments

18. Applicant's arguments with respect to claims 42, 45-52, 54-61, 64-66 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

19. No claims are allowed.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nelson Yang whose telephone number is (571)272-0826. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571)272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

21. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nelson Yang/
Patent Examiner, Art Unit 1641